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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/748,897	12/29/2003	Anthony Joonkyoo Yun	PALO-002	7432

24353 7590 02/22/2008

BOZICEVIC, FIELD & FRANCIS LLP
1900 UNIVERSITY AVENUE
SUITE 200
EAST PALO ALTO, CA 94303

EXAMINER	
RAMACHANDRAN, UMAMAHESWARI	
ART UNIT	PAPER NUMBER
1617	
MAIL DATE	DELIVERY MODE
02/22/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Advisory Action Before the Filing of an Appeal Brief	Application No. 10/748,897	Applicant(s) YUN ET AL.	
	Examiner UMAMAHESWARI RAMACHANDRAN	Art Unit 1617	

--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED 28 January 2008 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE.

1. ☒ The reply was filed after a final rejection, but prior to or on the same day as filing a Notice of Appeal. To avoid abandonment of this application, applicant must timely file one of the following replies: (1) an amendment, affidavit, or other evidence, which places the application in condition for allowance; (2) a Notice of Appeal (with appeal fee) in compliance with 37 CFR 41.31; or (3) a Request for Continued Examination (RCE) in compliance with 37 CFR 1.114. The reply must be filed within one of the following time periods:
   a) ☐ The period for reply expires _____months from the mailing date of the final rejection.
   b) ☒ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection.

   Examiner Note: If box 1 is checked, check either box (a) or (b). ONLY CHECK BOX (b) WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

NOTICE OF APPEAL

2. ☐ The Notice of Appeal was filed on _____. A brief in compliance with 37 CFR 41.37 must be filed within two months of the date of filing the Notice of Appeal (37 CFR 41.37(a)), or any extension thereof (37 CFR 41.37(e)), to avoid dismissal of the appeal. Since a Notice of Appeal has been filed, any reply must be filed within the time period set forth in 37 CFR 41.37(a).

AMENDMENTS

3. ☐ The proposed amendment(s) filed after a final rejection, but prior to the date of filing a brief, will not be entered because
   (a) ☐ They raise new issues that would require further consideration and/or search (see NOTE below);
   (b) ☐ They raise the issue of new matter (see NOTE below);
   (c) ☐ They are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or
   (d) ☐ They present additional claims without canceling a corresponding number of finally rejected claims.

   NOTE: _____. (See 37 CFR 1.116 and 41.33(a)).
4. ☐ The amendments are not in compliance with 37 CFR 1.121. See attached Notice of Non-Compliant Amendment (PTOL-324).
5. ☐ Applicant's reply has overcome the following rejection(s): _____.
6. ☐ Newly proposed or amended claim(s) _____ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).
7. ☒ For purposes of appeal, the proposed amendment(s): a) ☐ will not be entered, or b) ☒ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.
   The status of the claim(s) is (or will be) as follows:
   Claim(s) allowed: _____.
   Claim(s) objected to: _____.
   Claim(s) rejected: *1, 3, 4, 11-28, 41, 62, 63*.
   Claim(s) withdrawn from consideration: _____.

AFFIDAVIT OR OTHER EVIDENCE

8. ☐ The affidavit or other evidence filed after a final action, but before or on the date of filing a Notice of Appeal will not be entered because applicant failed to provide a showing of good and sufficient reasons why the affidavit or other evidence is necessary and was not earlier presented. See 37 CFR 1.116(e).
9. ☐ The affidavit or other evidence filed after the date of filing a Notice of Appeal, but prior to the date of filing a brief, will not be entered because the affidavit or other evidence failed to overcome all rejections under appeal and/or appellant fails to provide a showing a good and sufficient reasons why it is necessary and was not earlier presented. See 37 CFR 41.33(d)(1).
10. ☐ The affidavit or other evidence is entered. An explanation of the status of the claims after entry is below or attached.

REQUEST FOR RECONSIDERATION/OTHER

11. ☐ The request for reconsideration has been considered but does NOT place the application in condition for allowance because: _____.
12. ☐ Note the attached Information *Disclosure Statement*(s). (PTO/SB/08) Paper No(s). _____
13. ☒ Other: Please see Note.

/SREENI PADMANABHAN/
Supervisory Patent Examiner, Art Unit 1617

Note:

The amendments dated 1/28/2008 will be entered as there are no amendments to the claims.

Applicants' arguments regarding the rejections have been fully considered and found not persuasive. The rejections of record wil still be maintained as the claims are not allowable over prior art of record.

Claims 1, 3, 4, 13, 14, 16, 18-22, 28, 41, 62, 63 are rejected under 35 U.S.C. 103(a) as being unpatentable over Gambardella et al. (Metabolism, 46, 3, March, 1999, p 291-297). Gambardella teach a method of treating a condition deficient in parasympathetic activity in cancer patients by oral administration of propranolol. Gambardella teach that autonomic nervous system dysfunction in elderly cancer patients is rectified by the propranolol administration. Thus Gambardella teach the administration of the same drug, a beta blocker (propranolol) as claimed in the instant invention to the same overlapping patient population in a condition caused by an autonomic nervous system abnormality. It would have been obvious to one of ordinary skill in the art at the time of the invention from Gambardella's teachings that administration of propranolol modulates or alters the sympathetic and parasympathetic activities of the autonomic nervous system. Modulation of sympathetic and parasympathetic activities by a beta blocker such as propranolol is clearly a result effect parameter and it would have been obvious to one of ordinary skill in the art at the time of the invention that substantially equal parasympathetic and sympathetic functions can be reached by modulating such activities.

Claims 1, 3, 4, 21, 28, 41 are rejected under 35 U.S.C. 103(a) as being unpatentable over Brevetti et al. (Brief communications, Nov 1981, p 938-941). Brevetti et al. teach an intravenous and oral administration of propranolol for the treatment of Shy-Drager syndrome, a severe degeneration of the autonomic nervous system. The reference teaches a sympathetic bias and a parasympathetic bias in at least a portion of said autonomic nervous system. Thus the reference teach the administration of the same drug, a beta blocker (propranolol) as claimed in the instant invention to the same overlapping patient population in a condition caused by an autonomic nervous system abnormality. It would have been obvious to one of ordinary skill in the art at the time of the invention that administration of propranolol modulates or balances the sympathetic and parasympathetic activities of the autonomic nervous system by treating Shy-Drager syndrome condition and when balancing such activities a stage is reached where sympathetic and parasympathetic activities are substantially equal. Also, modulation of sympathetic and parasympathetic activities by a beta blocker such as propranolol is clearly a result effect parameter and it would have been obvious to one of ordinary skill in the art at the time of the invention that substantially equal parasympathetic and sympathetic functions can be reached by modulating such activities.

Claims 1, 21, are rejected under 35 U.S.C. 103(a) as being unpatentable over Nordling et al. (E Urol, 1992, 21, 328-331). Nordling et al. teach the administration of non-selective beta-adrenergic receptor antagonist propranolol reduced the urethral inflammation. The reference also teaches that severity of urethral inflammation was increased in spontaneous hypertensive rats, which have an increased sympathetic tone as compared to the normotensive rats. Hence by reducing urethral inflammation by administration of propranolol, sympathetic tone is decreased. Thus the reference teach the administration of the same drug, a beta blocker (propranolol) as claimed in the instant invention to the same overlapping patient population in a condition caused by an autonomic nervous system abnormality. It would have been obvious to one of ordinary skill in the art at the time of the invention that administration of propranolol modulates or alters the sympathetic and parasympathetic activities of the autonomic nervous system. Also, modulation of sympathetic and parasympathetic activities by a beta blocker such as propranolol is clearly a result effect parameter and it would have been obvious to one of ordinary skill in the art at the time of the invention that substantially equal parasympathetic and sympathetic functions can be reached by modulating such activities.

Claims 1, 3, 4, 11-12, 15, 17, 21, 22 are rejected under 35 U.S.C. 103(a) as being unpatentable over Majcherczyk et al. (Br J Pharmacol, 1987, 91(4), 711-4). Majcherczyk et al. teaches the increase in renal sympathetic nerve activity by propranolol in hypertensive rats (Abstract). Hypertension is an age-associated condition and the reference inherently teaches the sympathetic and non-sympathetic bias and a low sympathetic activity. It would have been obvious to one of ordinary skill in the art at the time of the invention that administration of propranolol modulates or alters the sympathetic and parasympathetic activities of the autonomic nervous system in the treatment of hypertension. Also, modulation of sympathetic and parasympathetic activities by a beta blocker such as propranolol is clearly a result effect parameter and it would have been obvious to one of ordinary skill in the art at the time of the invention that substantially equal parasympathetic and sympathetic functions can be reached by modulating such activities.

Claims 1, 21, 23-25, 28 are rejected under 35 U.S.C. 103(a) as being unpatentable over Davies et al. (The J of Intl Med Research, 1988, 16, 173-181). Davies et al. teach the administration of ibuprofen, a non-steroidal anti-inflammatory drug along with an anti-hypertensive agent and a beta-blocker such as propranolol to group of patients with hypertension. Thus the reference teach the administration of the same drug, a beta blocker (propranolol) as claimed in the instant invention to the same overlapping patient population in a condition caused by an autonomic nervous system abnormality. It would have been obvious to one of ordinary skill in the art at the time of the invention that administration of propranolol modulates or alters the sympathetic and parasympathetic activities of the autonomic nervous system in the treatment of hypertension. Hence it would have been obvious to one of ordinary skill in the art at the time of the invention that by modulating the parasympathetic nerves that influence cerebral blood flow during hypertension a substantially equal sympathetic and parasympathetic activities can be attained.

Claims 1, 26-27 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hill et al. (U.S. 6,449,507). Hill et al. teach the stimulation of nerve or nerve fibers (vagus nerve fibers, hypoglossal nerve fibers, phrenic nerve fibers, parasympathetic nerve fibers, and sympathetic nerve fibers, a vagal nerve) by using electrodes and electrical current and further comprising beta-blockers such as propranolol in a medical procedure such as beating heart surgery, arrythmias, vascular surgery, neurosurgery etc which are aging associated conditions (col. 2, lines 61-65, col. 17, claim 1, claim 10, col. 18, claim 19, co. 20, claim 50). It would have been obvious to one of ordinary skill in the art at the time of the invention that administration of propranolol modulates or alters the sympathetic and parasympathetic activities of the autonomic nervous system as Hill teaches the stimulation of parasympathetic and sympathetic nerve fibers. Hence it would have been obvious to one of ordinary skill in the art at the time of the invention that by modulating the stimulation of nerve fibers a substantially equal sympathetic and parasympathetic activities can be attained.